

CLAIMS

1. The use of a polypeptide comprising SEQ ID NO: 2 as a medicament.
- 5 2. The use according to claim 1 wherein the polypeptide further comprises an isoleucine at position 64 of SEQ ID NO: 2.
3. The use according to claim 1 or 2 further characterized in that said polypeptide does not contain a mutation in position 9, 10, or 13 in the corresponding
10 sequence of SEQ ID NO: 2 and SEQ ID NO: 4.
4. The use according to claim 1 or 2 further characterized in that said polypeptide contains, in the corresponding sequence of SEQ ID NO: 2 and SEQ ID NO: 4:
 - a) a Cysteine in position 8, 14, 17, or 77; or
 - 15 b) an Alanine or a Glycine in position 1.
5. The use of any of the claims from 1 to 4, wherein said polypeptide comprises the constant region of a human immunoglobulin heavy chain.
- 20 6. The use of a polypeptide comprising SEQ ID NO: 2 for the manufacture of a medicament for the treatment of autoimmune, inflammatory or infectious diseases.
7. The use according to claim 65 wherein the polypeptide further comprises an
25 isoleucine at position 64 of SEQ ID NO: 2.

8. The use according to claim 6 or 76 further characterized in that said polypeptide does not contain a mutation in position 9, 10, or 13 in the corresponding sequence of SEQ ID NO: 2 and SEQ ID NO: 4.

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9. The use according to claim 6 or 7 further characterized in that said polypeptide contains, in the corresponding sequence of SEQ ID NO: 2 and SEQ ID NO: 4:
- a) a Cysteine in position 8, 14, 17, or 77; or
 - b) an Alanine or a Glycine in position 1.

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10. The use of any of the claims from 6 to 9, wherein said polypeptide comprises the constant region of a human immunoglobulin heavy chain.

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11. The use according to claim 6 wherein said disease is selected from the group consisting of: arthritis, rheumatoid arthritis (RA), psoriatic arthritis, osteoarthritis, systemic lupus erythematosus (SLE), systemic sclerosis, scleroderma, polymyositis, glomerulonephritis, fibrosis, fibrosis, allergic or hypersensitivity diseases, dermatitis, asthma, chronic obstructive pulmonary disease (COPD), inflammatory bowel disease (IBD), Crohn's diseases, ulcerative colitis, multiple sclerosis, cancer, septic shock, viral or HIV infections, transplantation, , airways inflammation, graft-versus-host disease (GVHD) and atherosclerosis.

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12. The use according to claim 7 wherein said disease is selected from the group consisting of: arthritis, rheumatoid arthritis (RA), psoriatic arthritis, osteoarthritis, systemic lupus erythematosus (SLE), systemic sclerosis, scleroderma,

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polymyositis, glomerulonephritis, fibrosis, fibrosis, allergic or hypersensitivity diseases, dermatitis, asthma, chronic obstructive pulmonary disease (COPD), inflammatory bowel disease (IBD), Crohn's diseases, ulcerative colitis, multiple sclerosis, cancer, septic shock, viral or HIV infections, transplantation, , airways inflammation, graft-versus-host disease (GVHD) and atherosclerosis.

13. The use according to claim 11 wherein the disease is multiple sclerosis.

14. The use according to claim 12 wherein the disease is multiple sclerosis.

15. The fusion polypeptide amino acid sequence of SEQ ID NO: 2 fused to the constant region of a human immunoglobulin heavy chain of SEQ ID NO: 5.

16. The nucleic acid sequence encoding for the fusion polypeptide of SEQ ID NO: 5.

17. Method for producing the fusion polypeptide of claim 15 comprising:

- a) cloning of the nucleic acid sequence encoding the mature CCL2-P8A in an expression vector fused to a nucleic acid sequence encoding the human CCL2 signal sequence at its 5' end, and the nucleic acid sequence encoding the constant region (segment 243-474) of human immunoglobulin lambda heavy chain IgG1 at its 3' end;
- b) transforming a CHO or HEK293 cell line with the resulting vector;

- c) selecting the clones stably expressing and secreting the recombinant fusion protein having CCL2-P8A at the N-terminus and the IgG1 sequence at the C-terminus;
- d) purifying the fusion protein from the culture medium.

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18. Methods for screening for obligate monomeric antagonist chemokine variants described herein comprising:

- a) making single point mutations in CCL2 that block its ability to dimerize;
- b) identifying said variants that bind to the receptor and show agonistic properties in vitro;
- c) identifying said variants from the group identified in (b) above that are further characterized as inhibiting peritoneal cell recruitment.

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19. The pharmaceutical composition comprising a monomeric variant of a homodimer-forming chemokine as active ingredient, wherein said variant result from at least an amino acid substitution that alters the pattern of hydrogen bonds at the dimerization interface of said chemokine.

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20. The pharmaceutical composition of claim 19 wherein the monomeric variant is chosen from:

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- a) CCL2-P8A (SEQ ID NO: 2);
- b) CCL2*-P8A (SEQ ID NO: 4);
- c) An active mutant of (a) or (b); or
- d) A polypeptide comprising (a), (b), or (c), and an amino acid sequence belonging to a protein sequence other than said chemokine.

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21. The pharmaceutical composition of claim 18 or 19, wherein said monomeric variants is in the form of an active fraction, precursors, salt, derivative, complex or conjugate.
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22. A method for treating or preventing autoimmune, inflammatory, or infectious diseases comprising the administration of an effective amount of a monomeric variants of a homodimer-forming chemokine, wherein said variant result from at least an amino acid substitution that alters the pattern of hydrogen bonds at the
- 10 dimerization interface of said chemokine.
23. The method of claim 21 wherein the monomeric variant is chosen from:
- a) CCL2-P8A (SEQ ID NO: 2);
 - b) CCL2*-P8A (SEQ ID NO: 4);
 - 15 c) An active mutant of (a) or (b); or
 - d) A polypeptide comprising (a), (b), or (c), and an amino acid sequence belonging to a protein sequence other than said chemokine.